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Progress Report on Infants with Serious Cardiac Malformations

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Two aims of an inquiry into cardiovascular emergencies in the first year of life are to determine the incidence of malformations and to assess the prognosis, especially the changing prognosis which may be expected to reflect changing methods of management. The two are closely linked because any general conclusion reached on the subject of prognosis must take into account not only the diagnostic and therapeutic techniques available at the time, but also the incidence of remediable and irremediable malformations in the population. A previous survey (Coleman, 1965) disclosed that at the Royal Hospital for Sick Children, Glasgow, the relative incidence of malformations was not identical with that elsewhere, and also that the prognosis for this group of patients was so poor that more vigorous diagnostic and therapeutic measures were indicated. The present report reviews data from the same source obtained during subsequent years.

Clinical Material

All patients in the first year of life admitted to the Royal Hospital for Sick Children, Glasgow, during the 3-year period beginning October 1, 1962, because of cardiovascular disease with symptoms (breathlessness, cyanosis, congestive cardiac failure) were followed to the end of the first year of life or until death if this occurred earlier. Out of a total of 154 patients, the diagnosis in 29 was made by clinical, radiographic, and electrocardiographic examination only; in 125 this information was supplemented by evidence supplied by cardiac catheterization and angiocardiography (82), thoracotomy (38), or necropsy (67). A second group of patients, included to provide additional information, consisted of all those admitted with the same symptoms in the same age period during the 12 months which ended on March 31, 1968. In this group of 60 patients the diagnosis in 12 patients was made on the basis of clinical, radiographic, and electrocardiographic findings only, but was confirmed in 48 by cardiac catheterization and angiocardiography (39), thoracotomy (21), or necropsy (29).

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The term *net mortality* was used to express the percentage death rate when patients who had survived surgical operation were excluded from the calculation.

Medical measures employed in the management of infants suffering from congestive cardiac failure were digitalization, with diuretic therapy and dietary sodium restriction in addition where the response was poor or cardiac failure particularly severe. Infants were nursed in the upright position, and oxygen was administered according to the demands of the clinical situation.

Results

There was no significant difference between the numbers of male and female patients in the two groups. Of the 154 patients in the 1962–65 group, 78 were male and 76 were female; and of the 60 patients in the 1967–69 group, 32 were male and 28 were female. In the 1962–65 group the total number of deaths was 81 (52·5%), the number of deaths among males being 44 and among females 37; thus the death rate among male infants was 56 per cent and among female infants 48 per cent. Of 38 operations in the 1962–65 group, 25 were successful; thus the *net mortality* rate among the whole group of patients was 63 per cent.

Age and Urgency. Of the 1962–65 group, 80 per cent (123 patients) first attended hospital during the first 6 months of life, and 58 per cent (89) in the first 3 months. Seventy-eight per cent of all deaths (64) took place in the first 6 months of life, and 50 per cent (41) during the first 3 months. Twenty-three per cent of deaths (19) occurred within 7 days of the first visit to hospital and 10 per cent (8) within 24 hours.

Cyanosis. Cyanosis was a feature of 84 patients (54%) in the 1962–65 group, and 56 of these (67%) did not survive to the first birthday. Among

TABLE I

CHANCE OF SURVIVAL RELATED TO CYANOSIS AND CONGESTIVE CARDIAC FAILURE

Assessment at admission		Chance of survival to first birthday	
Cyanosis	Heart failure	1962–65 (154 patients)	1959–62 (166 patients)
Absent	Absent	4:1	3:1
Present	Absent	1:1	1:1
Absent	Present	1:1	0·3:1
Present	Present	0·25:1	0·1:1

TABLE II

MALFORMATIONS RESPONSIBLE FOR SYMPTOMS IN FIRST YEAR OF LIFE (1962–65) IN 131 (85%) OF 154 PATIENTS

Malformation	No. of patients	% of total
Ventricular septal defect	36	23
Complete transposition of great arteries	29	19
Preductal coarctation of aorta	18	11·5
Persistent ductus arteriosus	13	8·5
Fallot's tetralogy	11	7
Tricuspid atresia	7	4·5
Persistent ostium atrioventriculare commune	7	4·5
Endocardial fibro-elastosis	5	3
Pulmonary atresia	5	3

acyanotic patients, 25 out of 70 (36%) did not survive until the first birthday. Successful operations numbered 15 among the acyanotic, and 10 among the cyanotic; the *net mortality* rate was therefore 45 per cent and 76 per cent, respectively.

Congestive Cardiac Failure. Of the 1962–65 group, 84 patients (54%) were in established congestive cardiac failure when first referred to the hospital; of these, 58 (70%) died within the survey period. By contrast, only 23 (33%) died of 70 patients without congestive cardiac failure.

The chance of survival to the first birthday calculated from the presence or absence of cyanosis and congestive cardiac failure at the time of admission in the 1962–65 group was compared with the corresponding figures derived from the previous triennium (Coleman, 1965). The object of this was to examine the effect of improved methods of management on the chance of survival (Table I).

Principal Malformations. Multiple defects (other than those considered to be part of a compensatory mechanism) were common, particularly in association with ventricular septal defect and preductal coarctation of the aorta. Patients were classified in accordance with the defect that was considered, from the information available, to have had the greatest effect on circulatory haemodynamics. The first 9 malformations in order of frequency set out in Table II accounted for 85 per cent (131) of the 1962–65 group of patients. Four of these, namely ventricular septal defect, complete transposition of the great arteries, preductal coarctation of the aorta, and persistent ductus arteriosus, accounted for 62 per cent of the admissions. In Table III are listed the most common lesions in the 1962–65 group as compared with findings in 1967–68 and in 1959–62 (Coleman, 1965). The 4 malformations just mentioned were foremost during the entire 6-year period from 1959, but the order of those next in frequency changed. In 1967–68, however, the incidence of complete transposition of the great arteries fell from second to fifth in frequency. Among the causes of death recorded in 80 per cent of patients (Table IV) during 1962–65, complete transposition was foremost, with second and third places occupied by preductal coarctation and ventricular septal defect. These three malformations in a different order but with a closely similar percentage incidence had also headed the list in the 1959–62 period. As with the malformations causing symptoms, the fatal malformations next in frequency in 1962–65 were in a distinctly different order from those incriminated in 1959–62. Moreover, persistent truncus arteriosus, persistent ductus arteriosus, and total anomalous pulmonary venous drainage had been replaced in the table of common

TABLE III

PERCENTAGE INCIDENCE OF MALFORMATIONS CAUSING SYMPTOMS IN 1959–62, 1962–65, AND 1967–68 (9 MAIN LESIONS IN EACH PERIOD ARE SHOWN)

1959–62 (83%)		1962–65 (85%)		1967–68 (86%)	
Ventricular septal defect	25	Ventricular septal defect	23	Ventricular septal defect	30
Complete transposition	16	Complete transposition	19	Preductal coarctation	13
Preductal coarctation	9	Preductal coarctation	11·5	Fallot's tetralogy	8
Persistent ductus	8·5	Persistent ductus	8·5	Persistent ostium AV commune	8
Endocardial fibro-elastosis	6	Fallot's tetralogy	7	Complete transposition	7
Fallot's tetralogy	5	Tricuspid atresia	4·5	Persistent ductus	7
Persistent truncus	5	Persistent ostium AV commune	4·5	Persistent truncus	5
Tricuspid atresia	4	Endocardial fibro-elastosis	3	Mitral atresia	5
Total anomalous pulmonary venous drainage	4	Pulmonary atresia	3	Pulmonary atresia	3·5

fatal malformations by pulmonary atresia, Fallot's tetralogy, and persistent ostium atrioventriculare commune.

Progress in Management. The changing prognosis for these acutely ill patients is indicated in Table V. A more active approach to management became established late in 1964. A comparison of figures derived from experience in 1959–62, 1962–65, and 1967–68 indicates a close similarity in the yearly admission rate, but a twofold increase in the frequency of cardiac catheterization and angiocardiography and a 50 per cent increase in the number submitted to surgical treatment. Though during 1962–65 the proportion of surgical operations rated as successful had increased greatly over that of the previous 3 years, it declined during 1967–68 to a figure (43%) 4 per cent above that of 1959–62.

Patients Not Investigated by Cardiac Catheterization. During 1962–65, 49 patients died without cardiac catheterization and angiocardiography being performed; 22 died within one week, and most of these within 48 hours, of their first appearance at hospital; 12 had inoperable lesions, 2 suffered from mongolism, 2 died unexpectedly and rapidly in the course of an acute respiratory infection, and 4 had already sustained a major venous thrombosis (cerebral or renal) by the time of admission. Only two (Fallot's pentalogy, tricuspid atresia) seemed in retrospect to have been suitable for palliative therapy.

Of 27 who died a week or more after their first admission to hospital, 7 had inoperable anomalies, 1 suffered from mongolism, and 1 had sustained an extensive cerebral venous thrombosis. The remaining 16 patients might, however, have benefited from palliative surgical treatment if the diagnosis had been reached (complete transposition, complicated ventricular septal defect, Fallot's tetralogy, tricuspid atresia, total anomalous pulmonary venous drainage).

In all, 23 patients, who were subjected neither to cardiac catheterization nor to surgical treatment, survived to the end of the first year solely with medical treatment.

Patients Not Receiving Surgical Treatment. There were 19 patients who died having undergone cardiac catheterization and angiocardiography but without any form of surgical treatment. Seven were pronounced unsuitable for operation because of the nature of their defect (single ventricle, endocardial fibro-elastosis, pulmonary atresia) and one because of renal vein thrombosis. Bronchopneumonia was responsible for the death of 2 others. Among 9 regarded in retrospect as suitable for emergency surgical treatment were 7 with complete transposition and 2 with multiple anomalies including a ventricular septal defect and another shunt; operation in these instances was postponed at the time of cardiac catheterization because of the apparent well-being of the patients.

Thirty patients catheterized but not operated upon survived into their second year of life.

TABLE IV

PRINCIPAL MALFORMATIONS RESPONSIBLE FOR DEATH (1962–65) IN 65 (80%) OF 81 PATIENTS

Malformation	No. of patients	% of total
Complete transposition of great arteries	23	28·5
Preductal coarctation of aorta	14	17·5
Ventricular septal defect	12	15
Tricuspid atresia	4	5
Pulmonary atresia	3	3·5
Fallot's tetralogy	3	3·5
Endocardial fibro-elastosis	3	3·5
Persistent ostium atrioventriculare commune	3	3·5

TABLE V

NUMERICAL ASSESSMENT OF CHANGING MANAGEMENT (1959–68)

	1959–62	1962–65	1967–68
No. of patients admitted per year	55	51	60
Percentage of patients catheterized	31	53	62
Percentage of patients subjected to operation	23	25	35
Ratio of operations to catheterizations (%)	73	46	57
Ratio of successful operations to total operations (%)	39	66	43

Discussion

Congenital cardiovascular disease presenting with acute symptoms in the first year of life appears to affect both sexes almost equally, but to cause more deaths among boys. Further examination of the data has shown that this is largely accounted for by numerically important lesions such as preductal coarctation of the aorta and persistent ductus arteriosus being considerably more lethal to boys, though their incidence is higher among girls; both the incidence and the mortality rate for complete transposition were much higher among boys. Pulmonary hypertension, though more frequently recorded among girls, was more often associated with death among boys. The figures obtained relating to age at admission and at death merely confirm that the demand of congenital heart disease for urgent treatment is largely a feature of the earliest months of life, and that its capacity for causing

emergency clinical situations, with a high mortality, is four-fifths spent when the middle of the first year has passed.

The mortality and survival figures presented and compared here cover a span of approximately 9 years. The most recent figures disclose that the full range of investigation including cardiac catheterization and angiocardiography is now undertaken with increasing frequency. That these investigations are still being performed less often than is desirable is attributable largely to a fault in management, namely a failure to predict or to anticipate deterioration. Approximately one-third of the patients died within the week following admission to hospital, yet these were not all newborn infants, and symptoms had not in all cases appeared suddenly or only during recent days. Some infants desperately ill on admission had in fact been under medical supervision elsewhere, while in other cases their parents had not sought medical advice, being largely unaware of the presence of symptoms or of their significance. Many parents are strikingly oblivious to the presence of central cyanosis in their offspring even when severe. Most of those who had been under medical supervision had not been referred early because of an idea or hope, proved by events to have been mistaken, that spontaneous improvement was taking place or likely to take place. The not uncommon result of this over-optimistic view is that the infant is presented when undergoing rapid deterioration to the cardiological service; the best days of his life, now past, have been lived elsewhere, and he may be beyond help. There is no need nowadays to submit this group of patients to further clinical experiment in order to prove that many will soon die unless energetic treatment is available. Severe or increasing breathlessness, severe or increasing cyanosis, cyanotic attacks (unless brief, infrequent, and mild), congestive cardiac failure, all demand that full investigation be undertaken. If at any time the number of patients requiring a full diagnostic assessment is so great as to outstrip the facilities available for cardiac catheterization and angiocardiography, a standard clinical, radiographic, and electrocardiographic examination is almost invariably sufficient to allow a valid decision on priorities for cardiac catheterization, this decision being based on clinical urgency, and the probability or improbability of emergency operative treatment being available for the suspected malformation. The establishment of atrial septostomy among palliative measures in connexion with complete transposition of the great arteries and tricuspid atresia (Rashkind and Miller, 1966; Singh, Astley, and Parsons, 1968) has introduced a new aspect to the timing of diagnostic procedures. Unless the balloon septostomy can be performed early (first 6–8 weeks of life), the wide stellate rupture of the fossa ovalis, which is desired, will not be achieved, and only a much more limited and less beneficial splitting of the angles of the foramen ovale.

The number of patients subjected to surgical treatment did not rise so rapidly during the review period as the number submitted to cardiac catheterization. This was inevitable largely because the greater the proportion of acutely ill patients who are catheterized, the greater will be the number found to have an irremediable malformation. The ratio of operations to cardiac catheterizations fell sharply during the 1962–65 period from a higher level during 1959–62 to rise to a level intermediate between the two during the 1967–68 period. These fluctuations are accounted for by changes in the attitudes and skills of the physicians and surgeons concerned. The limited cardiac catheterization programme of the first period (1959–62) from which the most acutely ill were excluded meant that a high proportion of those investigated had apparently remediable lesions and were subjected to surgical treatment. In the second period (1962–65) very few extra of the larger number of patients investigated were accepted as suitable for surgical treatment, but this was now producing better results among the less desperately ill. During the last period (1967–68) more of the very ill patients investigated were accepted for surgical treatment with a consequent decline in the proportion of successful operations. In general terms it has been shown that surgical treatment has improved the prospects especially for patients in congestive cardiac failure, but also for acyanotic patients not in cardiac failure.

When the 1962–65 period is compared with 1959–62, there is a remarkable uniformity in the pattern of incidence of the leading malformations responsible for approximately 60 per cent of emergency admissions. Ventricular septal defect, complete transposition of the great arteries, preductal coarctation of the aorta, and persistent ductus arteriosus recur as the dominant lesions. The sharp decline in the incidence of complete transposition in the 1967–68 group is therefore particularly notable. Since the Royal Hospital for Sick Children is the principal hospital of reference for the community and remains in close association with the largest maternity hospitals, there is no reason or evidence for suspecting the transfer elsewhere of infants with complete transposition. This trough in the incidence of one malformation (not compensated for during the first half of the year 1968–69) was counterbalanced by an increase in the incidence of

certain other forms of cyanotic congenital heart disease. These changes may have been fortuitous, but it is noteworthy that the total percentage incidence of the several varieties of abnormal origin of the great arteries which are in some way associated with maldevelopment or faulty incorporation into the heart of the bulbo-truncal area (complete transposition, persistent truncus arteriosus, pulmonary atresia, Fallot's tetralogy, double outlet right ventricle) was virtually static throughout the entire period of these reviews. The possibility therefore suggested itself that this shift in incidence, from one common malformation to others all closely related in stage and site of embryological development, might represent a minor change in the character or timing of some teratogenic influence active at the 4–12 mm. stage of embryonic growth. Because of the high incidence of these malformations, any such teratogenic agent must be commonplace, indeed ubiquitous, within the community.

By the end of the triennium 1962–65 the three principal causes of death had remained unchanged for a period of 6 years, with complete transposition in the lead. Persistent ductus arteriosus had very properly ceased to be a frequent cause of death, having been eliminated by a more effective diagnostic service leading to early operation. Among the changes in the three years from 1962, persistent ostium atrioventriculare commune much increased in frequency, matching an increase in the number of patients with mongolism admitted because of cardiovascular symptoms.

When the present survey material is examined for information affecting survival statistics in the future, it seems probable that the high death rate from complete transposition of the great arteries is one that should be much reduced because of the introduction of atrial septostomy. The same consideration applies to some extent to tricuspid atresia where the judicious combination of this procedure with an anastomotic operation between the systemic and pulmonary arterial systems should improve the immediate prognosis. This same form of anastomosis is even more relevant to Fallot's tetralogy in those individuals with particularly severe obstruction of the right ventricular outlet, and to pulmonary atresia, in a sense the most extreme form of Fallot's tetralogy.

Attention has already been paid to the need to make an early diagnosis and to pursue the medical and surgical treatment with vigour if some of the many patients who at present die are to survive in the future. The frequent occurrence of intravascular thrombosis (renal and cerebral) leading to the death of several infants with severe cyanotic disease emphasizes that polycythaemia is a factor which in itself may constitute an indication for emergency operation after urgent investigations. There is little doubt from experience in this centre that a haemoglobin level of 20 g./100 ml. or above is potentially serious, and a case can be made for venesection whenever a sudden rise in intravascular osmolality is envisaged, as is entailed by angiocardiography.

A substantial number of patients survived the first year of life solely with medical treatment. Many had large arteriovenous shunts usually at ventricular level, often with an additional atrial septal defect. Their clinical improvement was probably attributable at least in part to spontaneous narrowing of the ventricular septal defect. Intractable congestive cardiac failure associated with a ventricular septal defect and pulmonary hypertension is an indication for pulmonary artery banding, but where there is a large atrial septal defect in addition, operation carries a greater risk and benefit resulting from it is less assured (Reid *et al.*, 1968).

A group of patients presenting a special problem consists of those for whom palliative surgery may prove life-saving, but for whom radical surgical treatment is not practicable at a later date. Tricuspid atresia after a Blalock-Taussig or Glenn anastomosis is a good example. Fallot's tetralogy after some transient benefit from a Blalock-Taussig or other systemic-pulmonary anastomosis, where as part of the right ventricular outlet obstruction the pulmonary artery is narrow to the bifurcation and beyond, or persistent truncus arteriosus after a bilateral pulmonary artery banding operation, illustrate the same point. It is essential to make as complete an assessment as possible of the anatomical and functional situation by cardiac catheterization and angiocardiography before the palliative operation. The parents must then be put in possession of the facts with regard both to the immediate intention and to future prospects before their consent to the immediate operation is requested. In this way it may be possible to prevent the later occurrence of the situation nowadays occasionally encountered when, after the child has begun to show progressive deterioration, the parents express regret that the earlier palliative operation should have been undertaken.

Summary

The immediate prognosis and the malformations are described in a series of 154 children who in the course of a 3-year period (1962–65) were admitted during the first year of life because of symptoms arising from congenital heart disease. An increasing number of patients subjected to full investigation and a gradually improving prognosis especially

for those admitted in congestive cardiac failure emerged from comparison with data derived both from earlier published experience and from 60 infants admitted in a recent 12-month period (1967–68). Improvement in prognosis is limited by the existence of complex and other irremediable malformations, and by the late appearance at hospital for diagnosis and treatment of patients at an advanced stage of deterioration. The malformations most frequently causing symptoms are complicated ventricular septal defects, complete transposition of the great arteries, preductal coarctation of the aorta, and persistent ductus arteriosus, but the incidence of complete transposition fell sharply during the latter part of the review period.

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